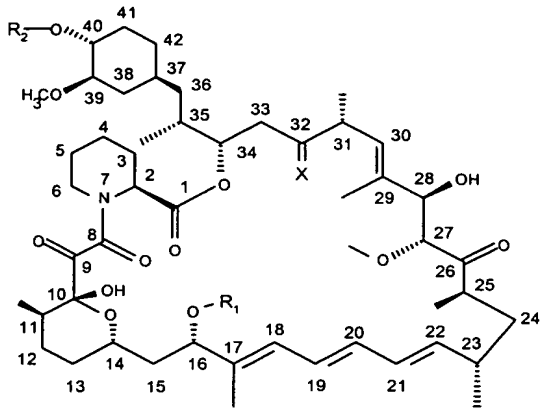
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1. (Canceled)

Claim 2. (Original): A pharmaceutical composition for use in the treatment of abnormally increased bone turnover or resorption comprising a rapamycin derivative of formula I



I

wherein

R_1 is CH_3 or C_{3-6}alkynyl,

R_2 is H or $-CH_2-CH_2-OH$, 3-hydroxy-2-(hydroxymethyl)-2-methyl-propanoyl or tetrazolyl, and X is =O, (H,H) or (H,OH),

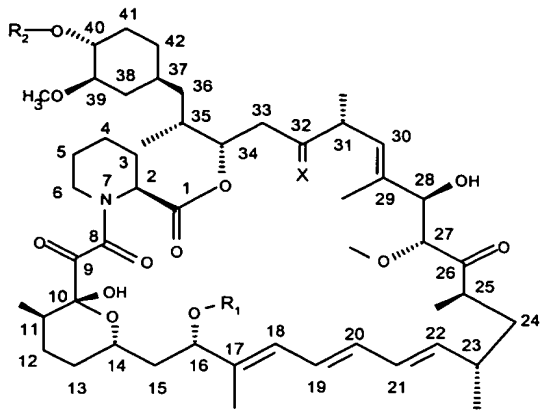
provided that R_2 is other than H when X is =O and R_1 is CH_3,

or a prodrug thereof when R_2 is $-CH_2-CH_2-OH$, e.g. a physiologically hydrolysable ether thereof,

together with one or more pharmaceutically acceptable diluents or carriers therefor.

Claim 3. (Original): A pharmaceutical combination comprising rapamycin or a rapamycin derivative and a second drug selected from bone resorption inhibitor, a calcitonin or an analogue or derivative thereof; a steroid hormone, a partial estrogen agonist or estrogen-gestagen combination; a selective estrogen receptor modulator; vitamin D or an analogue thereof; Parathyroid Hormone (PTH), a PTH fragment or a PTH derivative; a bisphosphonate; a cathepsin K inhibitor; a PTH releaser; a selective androgen receptor molecule; and strontium ranelate.

Claim 4. (Original): A method for treating abnormally increased bone turnover or resorption in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of a rapamycin derivative of formula I



I

wherein

R_1 is CH_3 or C_{3-6}alkynyl,

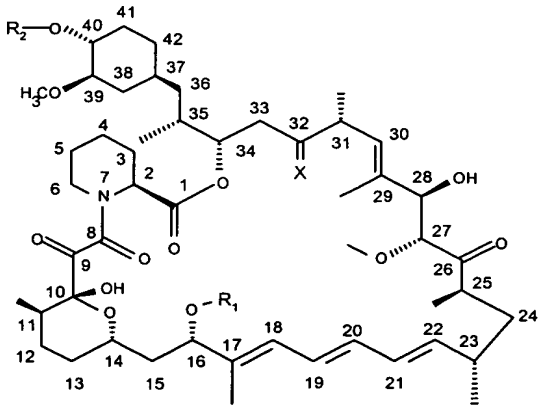
R_2 is H or $-CH_2-CH_2-OH$, 3-hydroxy-2-(hydroxymethyl)-2-methyl-propanoyl or tetrazolyl, and X is =O, (H,H) or (H,OH),

provided that R_2 is other than H when X is =O and R_1 is CH_3,

or a prodrug thereof when R_2 is $-CH_2-CH_2-OH$, e.g. a physiologically hydrolysable ether thereof.

Claim 5. (Original): A method for treating abnormally increased bone turnover or resorption in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of rapamycin or a rapamycin derivative, concomitantly or sequentially with a second drug selected from bone resorption inhibitor, a calcitonin or an analogue or derivative thereof; a steroid hormone, a partial estrogen agonist or estrogen-gestagen combination; a selective estrogen receptor modulator; vitamin D or an analogue thereof; Parathyroid Hormone (PTH), a PTH fragment or a PTH derivative; a bisphosphonate; a cathepsin K inhibitor; a PTH releaser; a selective androgen receptor molecule; and strontium ranelate.

Claim 6. (Currently amended): <u>The combination</u> ~~Combination~~ of claim 3 ~~or method according to claim 5~~ <u>containing a rapamycin derivative</u> wherein the rapamycin derivative is a compound of formula I



I

wherein

R_1 is CH_3 or C_{3-6}alkynyl,

R_2 is H or $-CH_2-CH_2-OH$, 3-hydroxy-2-(hydroxymethyl)-2-methyl-propanoyl or tetrazolyl, and X is =O, (H,H) or (H,OH),

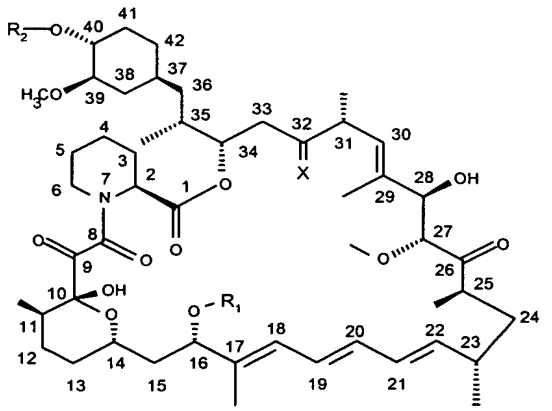
provided that R_2 is other than H when X is =O and R_1 is CH_3,

or a prodrug thereof when R_2 is $-CH_2-CH_2-OH$, e.g. a physiologically hydrolysable ether thereof.

Claim 7. (Currently amended): The ~~Use, composition, combination or method~~ according to ~~any preceding~~ claim 2 wherein the rapamycin derivative is selected from 40-O-(2-hydroxyethyl)-rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin, 40-epi-(tetrazolyl)-rapamycin, 32-deoxorapamycin, 16-pent-2-ynyloxy-32(S)-dihydro rapamycin, and TAFA-93.

Claim 8. (Currently amended): The ~~Use, composition, combination or method~~ according to ~~any preceding~~ claim 2 wherein the rapamycin derivative is 40-O-(2-hydroxyethyl)-rapamycin.

Claim 9. (Currently amended): A ~~Use, composition, combination or~~ method ~~according to any preceding claim~~ for the treatment of osteoporosis; bone loss secondary to or due to medication; bone loss associated with immobilisation and space flight; bone loss associated with rheumatoid arthritis, osteopenia, osteogenesis imperfecta, hyperthyroidism, anorexia nervosa, organ transplantation, joint prosthesis loosening; periarticular bone erosions in rheumatoid arthritis; osteoarthritis; hypercalcemia; bone cancer and bone metastases; and/or multiple myeloma, in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of rapamycin or a rapamycin derivative of formula I



I

wherein

R_1 is CH_3 or C_{3-6}alkynyl,

R_2 is H or $-CH_2-CH_2-OH$, 3-hydroxy-2-(hydroxymethyl)-2-methyl-propanoyl or tetrazolyl, and X is =O, (H,H) or (H,OH),

provided that R_2 is other than H when X is =O and R_1 is CH_3,

or a prodrug thereof when R_2 is $-CH_2-CH_2-OH$, e.g. a physiologically hydrolysable ether thereof,

concomitantly or sequentially with a second drug selected from bone resorption inhibitor, a calcitonin or an analogue or derivative thereof; a steroid hormone, a partial estrogen agonist or estrogen-gestagen combination; a selective estrogen receptor modulator; vitamin D or an analogue thereof; Parathyroid Hormone (PTH), a PTH fragment or a PTH derivative; a bisphosphonate; a cathepsin K inhibitor; a PTH releaser; a selective androgen receptor molecule; and strontium ranelate.

Claim 10. (New): The combination according to claim 3 containing a rapamycin derivative wherein the rapamycin derivative is selected from 40-O-(2-hydroxyethyl)-rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin, 40-epi-(tetrazolyl)-rapamycin, 32-deoxorapamycin, 16-pent-2-ynyloxy-32(S)-dihydro rapamycin, and TAFA-93.

Claim 11. (New): The combination according to claim 3 containing a rapamycin derivative wherein the rapamycin derivative is 40-O-(2-hydroxyethyl)-rapamycin.

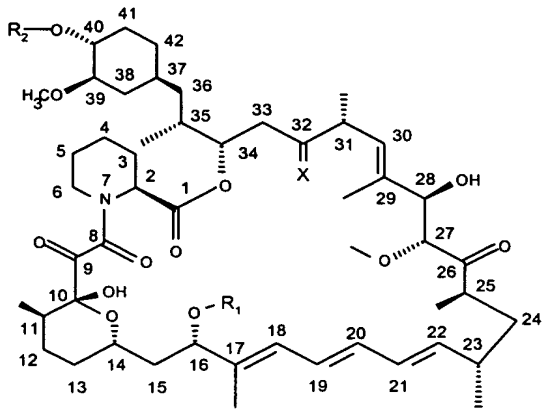
Claim 12. (New): The method according to claim 4 wherein the rapamycin derivative is selected from 40-O-(2-hydroxyethyl)-rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin, 40-epi-(tetrazolyl)-rapamycin, 32-deoxorapamycin, 16-pent-2-ynyloxy-32(S)-dihydro rapamycin, and TAFA-93.

Claim 13. (New): The method according to claim 4 wherein the rapamycin derivative is 40-O-(2-hydroxyethyl)-rapamycin.

Claim 14. (New): The method according to claim 9 wherein the rapamycin derivative is selected from 40-O-(2-hydroxyethyl)-rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin, 40-epi-(tetrazolyl)-rapamycin, 32-deoxorapamycin, 16-pent-2-ynyloxy-32(S)-dihydro rapamycin, and TAFA-93.

Claim 15. (New): The method according to claim 9 wherein the rapamycin derivative is 40-O-(2-hydroxyethyl)-rapamycin.

Claim 16. (New): The method according to claim 5 wherein the rapamyin derivative is a compound of formula I



wherein

R_1 is CH_3 or C_{3-6}alkynyl,

R_2 is H or $-CH_2-CH_2-OH$, 3-hydroxy-2-(hydroxymethyl)-2-methyl-propanoyl or tetrazolyl, and X is =O, (H,H) or (H,OH),

provided that R_2 is other than H when X is =O and R_1 is CH_3,

or a prodrug thereof when R_2 is $-CH_2-CH_2-OH$, e.g. a physiologically hydrolysable ether thereof.

Claim 17. (New): The method according to claim 5 wherein the rapamycin derivative is selected from 40-O-(2-hydroxyethyl)-rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin, 40-epi-(tetrazolyl)-rapamycin, 32-deoxorapamycin, 16-pent-2-ynyloxy-32(S)-dihydro rapamycin, and TAFA-93.

Claim 18. (New): The method according to claim 5 wherein the rapamycin derivative is 40-O-(2-hydroxyethyl)-rapamycin.